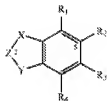


Claims Listing

1. (original) A method of inhibiting cytokine or biological activity of MIF comprising contacting MIF with a cytokine or biological activity inhibiting effective amount of a compound of formula (I), or a pharmaceutically acceptable salt or prodrug thereof



(I)

wherein X is selected from —O—, —S—, —C(R₅)(R₅)— or —N(R₆)—; Y is selected from —N(R₇)—, —O—, —S— or —C(R₇)₂—; Z is selected from —C(O)—, —C(S)—, —C(=NR₆)—, —S(O)— or —S(O)₂—; R₁ is selected from hydrogen, C₁₋₃alkyl, (CR₅R₅)_nOR₇, (CR₅R₅)_nSR₇, (CR₅R₅)_nN(R₆)₂ and (CR₅R₅)_nhalo; R₂ is selected from C₁-C₂₀alkyl, C₂-C₂₀alkenyl, C₂-C₂₀alkynyl, (CR₁₂R₁₂)_mC(O)R₈, (CR₁₂R₁₂)_mC(S)R₈, (CR₁₂R₁₂)_mS(O)R₈, (CR₁₂R₁₂)_mS(O)₂R₈, (CR₁₂R₁₂)_mOR₉, (CR₁₂R₁₂)_mSR₉, (CR₁₂R₁₂)_nNR₁₀R₁₁, (CR₁₂R₁₂)_mC(=NR₂₄)R₂₂ and (CR₁₂R₁₂)_mR₁₃; R₃ is selected from hydrogen, C₁-C₆alkyl, (CR₁₆R₁₆)_pNR₁₄R₁₅, (CR₁₆R₁₆)_pOR₁₇, (CR₁₆R₁₆)_pSR₁₇, (CR₁₆R₁₆)_phalo, (CR₁₆R₁₆)_pNO₂, (CR₁₆R₁₆)_nC(O)R₂₈, (CR₁₆R₁₆)_nC(=NR₂₄)R₂₂, (CR₁₆R₁₆)_nS(O)R₁₇, (CR₁₆R₁₆)_nS(O)₂R₁₇, (CR₁₆R₁₆)_nS(O)₃R₁₇ and (CR₁₆R₁₆)_pC(R₁₈)₃; R₄ is selected from hydrogen, halogen C₁-C₃alkyl, C₂₋₃alkenyl, C₂₋₃alkynyl and (CR₁₂R₁₂)_nC(R₁₈)₃; Each R₅ and R₅ is independently selected from hydrogen, C₁-C₃alkyl, halo, OR₇, SR₇ and N(R₆)₂; Each R₆ is independently selected from hydrogen, C₁-C₃alkyl and OR₇; Each R₇ is independently selected from hydrogen and C₁-C₃alkyl; R₈ is selected from hydrogen, C₁-C₂₀alkyl, C₂-C₂₀alkenyl, C₂-C₂₀alkynyl, OR₁₉, SR₁₉, N(R₂₀)₂, [NH—CH(R₂₁)—C(O)]_q—OR₂₉, [sugar]_q and (CR₁₂R₁₂)_nR₁₃; R₉ is selected from hydrogen, C₁-C₂₀alkyl, C₂-C₂₀alkenyl, C₂-C₂₀alkynyl,

$(\text{CR}_{12}\text{R}_{12'})_q\text{R}_3$, $\text{C}(\text{O})\text{R}_{23}$, CO_2R_{23} , $\text{C}(\text{S})\text{R}_{23}$, $\text{C}(\text{S})\text{OR}_{23}$, $\text{S}(\text{O})\text{R}_{23}$, $\text{S}(\text{O})_2\text{R}_{23}$, $[\text{C}(\text{O})\text{CH}(\text{R}_{21})\text{NH}]_q-$
 R_{23} and $[\text{sugar}]_q$; R_{10} and R_{11} are independently selected from hydrogen, C_1 - C_{20} alkyl, C_2 -
 C_{20} alkenyl, C_2 - C_{20} alkynyl, $(\text{CR}_{12}\text{R}_{12'})_m\text{R}_{13}$, $\text{C}(\text{O})\text{R}_{23}$, $\text{C}(\text{S})\text{R}_{23}$, $\text{S}(\text{O})\text{R}_{23}$, $\text{S}(\text{O})_2\text{R}_{23}$,
 $[\text{C}(\text{O})\text{CH}(\text{R}_{21})\text{NH}]_q-\text{R}_{23}$, $-\text{[sugar]}_q$ and $\text{NHC}(=\text{NR}_{25})-\text{NH}_2$; Each R_{12} and $\text{R}_{12'}$ is independently
selected from hydrogen, C_1 - C_6 alkyl, C_2 - C_6 alkenyl, C_2 - C_6 alkynyl, OR_{24} , SR_{24} , halo, $\text{N}(\text{R}_{24})_2$,
 CO_2R_{24} , CN , NO_2 , aryl or heterocyclyl; R_{13} is selected from OR_{25} , SR_{25} , halo, $\text{N}(\text{R}_{25})_2$, $\text{C}(\text{O})\text{R}_{31}$,
 CN , $\text{C}(\text{R}_{18})_3$, aryl or heterocyclyl; R_{14} and R_{15} are independently selected from hydrogen, C_1 -
 C_3 alkyl, OR_{17} , $(\text{CR}_{16}\text{R}_{16'})_p\text{C}(\text{R}_{18})_3$; Each R_{16} and $\text{R}_{16'}$ is independently selected from hydrogen,
 C_1 - C_3 alkyl, halo, OR_{17} , SR_{17} and $\text{N}(\text{R}_{17})_2$; Each R_{17} is independently selected from hydrogen and
 C_1 - C_3 alkyl; Each R_{18} is independently selected from hydrogen and halo; R_{19} and each R_{20} are
independently selected from hydrogen, C_1 - C_{20} alkyl, C_2 - C_{20} alkenyl, C_2 - C_{20} alkynyl,
 $(\text{CR}_{26}\text{R}_{26'})_t\text{R}_{27}$; R_{21} is the characterising group of an amino acid; R_{22} is selected from C_1 - C_6 alkyl,
 NH_2 , $\text{NH}(\text{C}_{1-6}\text{alkyl})$, $\text{N}(\text{C}_{1-6}\text{alkyl})_2$, OR_{29} or SR_{29} ; R_{23} is selected from hydrogen, C_1 - C_{20} alkyl, C_2 -
 C_{20} alkenyl, C_2 - C_{20} alkynyl, aryl $(\text{CR}_{26}\text{R}_{26'})_t\text{R}_{27}$; Each R_{24} is independently selected from hydrogen
and C_1 - C_6 alkyl; Each R_{25} is independently selected from hydrogen, C_1 - C_6 alkyl, C_{1-3} alkoxy C_{1-}
 3 alkyl, aryl and heterocyclyl; Each R_{26} and $\text{R}_{26'}$ is independently selected from hydrogen, C_1 -
 C_6 alkyl, C_2 - C_6 alkenyl, C_2 - C_6 alkynyl, OR_{29} , SR_{29} , halo, $\text{N}(\text{R}_{29})_2$, CO_2R_{29} , CN , NO_2 , aryl and
heterocyclyl; R_{27} is selected from hydrogen, OR_{30} , SR_{30} , halo, $\text{N}(\text{R}_{30})_2$, CO_2R_{30} , aryl and
heterocyclyl; R_{28} is selected from hydrogen, C_{1-6} alkyl, OR_{29} , SR_{29} or $\text{N}(\text{R}_{29})_2$; Each R_{29} is
independently selected from hydrogen and C_1 - C_3 alkyl; Each R_{30} is independently selected from
hydrogen, C_1 - C_3 alkyl, aryl and heterocyclyl; R_{31} is selected from C_{1-3} alkyl, OH , C_{1-3} alkoxy, aryl,
aryloxy, heterocyclyl and heterocyclyloxy; n is 0 or an integer from 1 to 3; m is 0 or an integer
from 1 to 20; p is 0 or an integer from 1 to 6; q is an integer from 1 to 5; t is an integer from 1 to

10; wherein alkyl, alkenyl, alkynyl, aryl and heterocyclyl may be optionally substituted.

2. (original) A method according to claim 1 wherein X is selected from the group consisting of —N(H)— , $\text{—N(C}_{1-3}\text{alkyl)—}$, —N(OH)— , $\text{—N(OC}_{1-3}\text{alkyl)—}$, —O— , —S— , $\text{—CH}_2\text{—}$, —CH(OH)— , $\text{—CH(NH}_2\text{)—}$, $\text{—CH(C}_{1-3}\text{alkyl)—}$, —CH(halo)— , —CH(SH)— , $\text{—CH(OC}_{1-3}\text{alkyl)—}$, $\text{—CH(SC}_{1-3}\text{alkyl)—}$.

3. (original) A method according to claim 1 wherein Y is selected from the group consisting of —NH— , —O— , —S— , $\text{—N(C}_{1-3}\text{alkyl)—}$ or $\text{—CH}_2\text{—}$.

4. (original) A method according to claim 1 wherein Z is selected from the group consisting of —C(O)— , —C(S)— , —C(=NH)— , $\text{—C(=NC}_{1-3}\text{alkyl)—}$, —C(=NOH)— or $\text{—C(=NOC}_{1-3}\text{alkyl)—}$.

5. (original) A method according to claim 1 wherein R₁ is selected from the group consisting of hydrogen, CH₃, OH, SH, NH₂, NHCH₃, F, Cl or Br.

6. (original) A method according to claim 1 wherein R₂ is selected from the group consisting of C₁₋₂₀alkyl, C₁₋₂₀alkenyl, (CR₁₂R_{12'})_mheterocyclyl, (CR₁₂R_{12'})_maryl, (CR₁₂R_{12'})_mhalo, (CR₁₂R_{12'})_mOH, (CR₁₂R_{12'})_mOC₁₋₂₀alkyl, (CR₁₂R_{12'})_mOC₂₋₂₀alkenyl, (CR₁₂R_{12'})_mOC(O)C₁₋₂₀alkyl, (CR₁₂R_{12'})_mOC(O)C₂₋₂₀alkenyl, (CR₁₂R_{12'})_mOC(O)aryl, (CR₁₂R_{12'})_mO[C(O)CH(R₂₁)NH]_r—H, (CR₁₂R_{12'})_mO[sugar]_r, (CR₁₂R_{12'})_mNH₂, (CR₁₂R_{12'})_mNHC₁₋₂₀alkyl, (CR₁₂R_{12'})_mN(C₁₋₂₀alkyl)₂, (CR₁₂R_{12'})_mNHC₂₋₂₀alkenyl, (CR₁₂R_{12'})_mN(C₂₋₂₀alkenyl)₂, (CR₁₂R_{12'})_mN(C₁₋₂₀alkyl)(C₂—

$_{20}\text{alkenyl}$), $(\text{CR}_{12}\text{R}_{12'})_m\text{NHC}(\text{O})\text{C}_{1-20}\text{alkyl}$, $(\text{CR}_{12}\text{R}_{12'})_m\text{NHC}(\text{O})\text{C}_{2-20}\text{alkenyl}$,
 $(\text{CR}_{12}\text{R}_{12'})_n\text{NHC}(\text{O})\text{aryl}$, $(\text{CR}_{12}\text{R}_{12'})_m\text{NH}[\text{C}(\text{O})\text{CH}(\text{R}_{21})\text{NH}]_r\text{—H}$, $(\text{CR}_{12}\text{R}_{12'})_m\text{NH}\text{—}[\text{sugar}]_r$,
 $(\text{CR}_{12}\text{R}_{12'})_m\text{SO}_3\text{H}$, $(\text{CR}_{12}\text{R}_{12'})_m\text{SO}_3\text{C}_{1-20}\text{alkyl}$, $(\text{CR}_{12}\text{R}_{12'})_m\text{SO}_3\text{C}_{2-20}\text{alkenyl}$, $(\text{CR}_{12}\text{R}_{12'})_m\text{C}(\text{O})\text{C}_{1-}$
 $_{20}\text{alkyl}$, $(\text{CR}_{12}\text{R}_{12'})_m\text{C}(\text{O})\text{C}_{2-20}\text{alkenyl}$, $(\text{CR}_{12}\text{R}_{12'})_m\text{CO}_2\text{H}$, $(\text{CR}_{12}\text{R}_{12'})_m\text{CO}_2\text{C}_{1-20}\text{alkyl}$,
 $(\text{CR}_{12}\text{R}_{12'})_m\text{CO}_2\text{C}_{2-20}\text{alkenyl}$, $(\text{CR}_{12}\text{R}_{12'})_m\text{C}(\text{O})\text{NHC}_{1-20}\text{alkyl}$, $(\text{CR}_{12}\text{R}_{12'})_m\text{C}(\text{O})\text{N}(\text{C}_{1-20}\text{alkyl})_2$,
 $(\text{CR}_{12}\text{R}_{12'})_m\text{C}(\text{O})\text{NHC}_{2-20}\text{alkenyl}$, $(\text{CR}_{12}\text{R}_{12'})_n\text{C}(\text{O})\text{N}(\text{C}_{2-20}\text{alkenyl})_2$, $(\text{CR}_{12}\text{R}_{12'})_m\text{C}(\text{O})\text{N}(\text{C}_{1-}$
 $_{20}\text{alkyl})(\text{C}_{2-20}\text{alkenyl})$, $(\text{CR}_{12}\text{R}_{12'})_m\text{C}(\text{O})[\text{NHCH}(\text{R}_{21})\text{C}(\text{O})]_r\text{—OH}$,
 $(\text{CR}_{12}\text{R}_{12'})_m\text{C}(\text{O})[\text{NHCH}(\text{R}_{21})\text{C}(\text{O})]_r\text{—OCH}_3$, $(\text{CR}_{12}\text{R}_{12'})_m\text{C}(\text{O})[\text{sugar}]_r$, $(\text{CR}_{12}\text{R}_{12'})_m\text{SC}_{1-6}\text{alkyl}$,
 $\text{C}(\equiv\text{N})\text{NHC}_{1-6}\text{alkyl}$; wherein each R_{12} and $\text{R}_{12'}$ is independently selected from hydrogen, C_{1-}
 $_{6}\text{alkyl}$, $\text{C}_{2-6}\text{alkenyl}$, $\text{C}_{2-6}\text{alkynyl}$, halogen, OH, hydroxy $\text{C}_{1-6}\text{alkyl}$, $\text{OC}_{1-6}\text{alkyl}$, CO_2H , CO_2C_{1-}
 $_{3}\text{alkyl}$, NH_2 , $\text{NHC}_{1-3}\text{alkyl}$, $\text{N}(\text{C}_{1-3}\text{alkyl})_2$, CN, NO_2 , aryl or heterocyclyl; R_{21} is the characterising
group of an amino acid, m is 0 or an integer from 1 to 20 and r is an integer from 1 to 5.

7. (original) A method according to claim 1 wherein R_3 is selected from the group consisting of hydrogen, halogen, $\text{C}_{1-6}\text{alkyl}$, $\text{—}(\text{CH}_2)_n\text{NH}_2$, $\text{—}(\text{CH}_2)_n\text{NO}_2$, $\text{—}(\text{CH}_2)_n\text{—OH}$, $\text{—}(\text{CH}_2)_n\text{—CF}_3$ or $\text{—}(\text{CH}_2)_n\text{—SH}$ wherein n is as defined in claim 1.

8. (original) A method according to claim 1 wherein R_4 is selected from the group consisting of hydrogen, methyl, ethyl, $\text{—CH}_2\text{=CH}_2$, CH_2CF_3 , fluoro, chloro or bromo.

9. (original) A method according to claim 1 wherein at least one of R_5 and $\text{R}_{5'}$ in each $(\text{CR}_5\text{R}_{5'})$ is hydrogen.

10. (original) A method according to claim 1 wherein at least one of R_{12} and $R_{12'}$ in each $(CR_{12}R_{12'})$ is hydrogen.

11. (original) A method according to claim 1 wherein at least one of R_{16} and $R_{16'}$ in each $(CR_{16}R_{16'})$ is hydrogen.

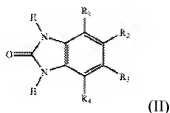
12. (original) A method according to claim 1 wherein at least one of R_{26} and $R_{26'}$ in each $(CR_{26}R_{26'})$ is hydrogen.

13. (original) A method according to claim 1 wherein X is selected from the group consisting of $-O-$, $-S-$, $-C(R_5)_2-$ or $-N(R_6)-$; Y is selected from the group consisting of $-N(R_7)-$, $-O-$, $-S-$, or $-C(R_7)_2-$; Z is selected from the group consisting of $-C(O)-$, $-C(S)-$, $-S(O)-$ or $-C(=NR_6)-$; R_1 is selected from the group consisting of hydrogen, CH_3 , OH, SH, NH_2 , $NHCH_3$, F, Cl or Br; R_2 is selected from the group consisting of C_1 - C_{20} alkyl, C_2 - C_{20} alkenyl, C_2 - C_{20} alkynyl, $(CR_{12}R_{12'})_mC(O)R_8$, $-(CR_{12}R_{12'})_mC(S)R_8$, $-(CR_{12}R_{12'})_mS(O)R_8$, $-(CR_{12}R_{12'})_mS(O)_2R_8$, $-(CR_{12}R_{12'})_mOR_9$, $-(CR_{12}R_{12'})_mSR_9$, $-(CR_{12}R_{12'})_mNR_{10}R_{11}$, $(CR_{12}R_{12'})_mC(=NR_{24})R_{22}$ or $(CR_{12}R_{12'})_mR_{13}$ where m, R_7 , R_8 , R_9 , R_{10} , R_{11} , R_{12} , $R_{12'}$, R_{13} , R_{22} and R_{24} are as defined in claim 1; R_3 is hydrogen, halogen, C_{1-6} alkyl, $-(CH_2)_nNH_2$, $-(CH_2)_nNO_2$, $-(CH_2)_nOH$, $-(CH_2)_nCF_3$ or $-(CH_2)_nSH$ where n is as defined in claim 1; and R_4 is hydrogen, halogen, methyl, ethyl, CH_2CF_3 or $-CH_2=CH_2$.

14. (original) A method according to claim 1 wherein X is $-N(R_6)-$; Y is $-N(R_7)-$ or $-C(R_7)_2-$; Z is $-C(O)-$, $-C(S)-$, $-S(O)-$ or $-C(=NH)-$; R_1 is hydrogen,

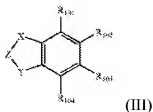
CH₃, NH₂, NHCH₃, F, Cl or Br; R₂ is as defined in claim 1; R₃ is hydrogen, halogen, C₁₋₃alkyl, (CH₂)_nNH₂, —(CH₂)_nNO₂, (CH₂)_nOH or (CH₂)_nCF₃ where n is defined in claim 1; and R₄ is hydrogen, halogen, methyl, ethyl, CH₂CF₃ or —CH₂=CH₂.

15. (original) A method according to claim 1 wherein the compound of formula (I) is a benzimidazole compounds having the formula (II):



wherein R₁ is hydrogen, CH₃, NHCH₃, F, Cl or Br; R₂ is as defined in claim 1; R₃ is hydrogen, halogen, C₁₋₃alkyl, (CH₂)_nNH₂, —(CH₂)_nNO₂, (CH₂)_nOH, CH₂C(O)CH₃, or (CH₂)_nCF₃ where n is as defined in claim 1; and R₄ is hydrogen, F, Cl or Br, methyl, ethyl, CH₂CF₃ or —CH₂=CH₂.

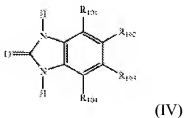
16. (original) A method according to claim 1 wherein the compound of formula (I) is a compound of formula (III):



wherein X is —O—, —NH— or —CH₂—; Y is —NH—, —O—, —S— or —CH₂—; Z is —C(O)—, —C(S)— or —S(O)—; R₁₀₁ is selected from hydrogen, C₁₋₃alkyl, OH, SH, NH₂, NHC₁₋₃alkyl, F, Cl or Br; R₁₀₂ is selected from C₁₋₂₀alkyl, C₂₋₂₀alkenyl, CO₂H, CO₂R₁₀₅, —NH₂, F, Cl,

Br, $(\text{CH}_2)_w\text{R}_{106}$, $\text{C}(\text{O})\text{N}(\text{R}_{107})_2$, $\text{C}(=\text{N})\text{NHC}_{1-6}\text{alkyl}$, $\text{SO}_2\text{C}_{1-6}\text{alkyl}$, $\text{C}(\text{O})[\text{NHCH}(\text{R}_{108})\text{C}(\text{O})]_q\text{—}$
OR₁₀₉, $\text{C}(\text{O})\text{sugar}$, $\text{CONH}(\text{CH}_2)_n\text{aryl}$, $\text{NHC}(\text{O})(\text{CH}_2)_n\text{Sheterocyclyl}$, $\text{C}(\text{O})\text{SC}_{1-6}\text{alkyl}$,
 $\text{C}(\text{O})(\text{CH}_2)_n\text{CO}_2\text{H}$, $\text{SO}_2\text{OC}_{1-10}\text{alkyl}$, and $\text{SO}_2\text{NHC}_{1-10}\text{alkyl}$; R_{103} is selected from hydrogen, F, Cl,
Br, $\text{C}_{1-}\text{alkyl}$, $\text{—}(\text{CH}_2)_n\text{NH}_2$, $\text{—}(\text{CH}_2)_n\text{NO}_2$, $\text{—}(\text{CH}_2)_n\text{—OH}$, $\text{—}(\text{CH}_2)_n\text{—CF}_3$, $\text{—}(\text{CH}_2)_n\text{C}(\text{O})\text{C}_{1-}$
 3alkyl or $\text{—}(\text{CH}_2)_n\text{—SH}$; R_{104} is selected from hydrogen, methyl, ethyl, $\text{CH}_2\text{C}(\text{R}_{110})_3$, $\text{C}(\text{R}_{110})_3$,
 $\text{—CH}_2\text{=CH}_2$, fluoro, chloro or bromo; R_{105} is selected from hydrogen, $\text{C}_{1-20}\text{alkyl}$, $\text{C}_{2-20}\text{alkenyl}$ or
 $(\text{CH}_2)_t\text{OC}_{1-3}\text{alkyl}$; R_{106} is selected from SH, $\text{SC}_{1-6}\text{alkyl}$, OH, $\text{OC}_{1-6}\text{alkyl}$, sugar, CO_2H , NH_2 ,
heterocyclyl or aryl; Each R_{107} is independently selected from hydrogen, $\text{C}_{1-20}\text{alkyl}$, $\text{C}_{2-20}\text{alkenyl}$,
 $(\text{CH}_2)_t\text{aryl}$ and $(\text{CH}_2)_t\text{heterocyclyl}$; R_{108} is the characterising group of an amino acid; R_{109} is
hydrogen, $\text{C}_{1-3}\text{alkyl}$; Each R_{110} is independently selected from hydrogen and halo; and n is 0 or
an integer from 1 to 3, q is an integer from 1 to 5, w is an integer from 1 to 6; t is an integer from
1 to 10; wherein each alkyl, alkenyl, alkynyl, aryl and heterocyclyl may be optionally
substituted.

17. (original) A method according to claim 1 wherein the compound of formula 1 is a
compound of formula (IV):



wherein R_{101} is selected from hydrogen, CH_3 , OH, SH, NH_2 , NHCH_3 , F, Cl or Br; R_{102} is selected
from $\text{C}_{1-20}\text{alkyl}$, $\text{C}_{2-20}\text{alkenyl}$, CO_2H , $\text{CO}_2\text{R}_{105}$, —NH_2 , F, Cl, Br, $(\text{CH}_2)_w\text{R}_{106}$, $\text{C}(\text{O})\text{N}(\text{R}_{107})_2$,
 $\text{C}(=\text{N})\text{NHC}_{1-6}\text{alkyl}$, $\text{SO}_2\text{C}_{1-6}\text{alkyl}$, $\text{C}(\text{O})[\text{NHCH}(\text{R}_{108})\text{C}(\text{O})]_q\text{—OR}_{109}$, $\text{C}(\text{O})\text{sugar}$,

CONH(CH₂)_naryl, NHC(O)(CH₂)_nSheterocyclyl, C(O)SC₁₋₆alkyl, C(O)(CH₂)_nCO₂H, SO₂OC₁₋₁₀alkyl, and SO₂NHC₁₋₁₀alkyl; R₁₀₃ is selected from hydrogen, F, Cl, Br, C₁₋₆alkyl, (CH₂)_nNH₂, —(CH₂)_nNO₂, —(CH₂)_n—CF₃, CH₂C(O)CH₃ or —(CH₂)_n—SH; R₁₀₄ is selected from hydrogen, methyl, ethyl, CH₂CF₃, —CH₂=CH₂ fluoro, chloro or bromo; R₁₀₅ is selected from hydrogen, C₁₋₁₀alkyl, C₂₋₁₀alkenyl, (CH₂)_nOC₁₋₃alkyl; R₁₀₆ is selected from SH, SC₁₋₆alkyl, OH, OC₁₋₆alkyl, sugar, CO₂H, NH₂, heterocyclyl or aryl; Each R₁₀₇ is independently selected from hydrogen, C₁₋₁₀alkyl, C₂₋₁₀alkenyl, (CH₂)_naryl and (CH₂)_nheterocyclyl; R₁₀₈ is the characterising group of an amino acid; R₁₀₉ is hydrogen, C₁₋₃alkyl; Each R₁₁₀ is independently selected from hydrogen and halo; and n is 0 or an integer from 1 to 3, q is an integer from 1 to 5, w is an integer from 1 to 6, t is an integer from 1 to 10; wherein each alkyl, alkenyl, alkynyl, aryl and heterocyclyl may be optionally substituted.

18. (original) A method according to claim 1 wherein the compound of formula 1 is selected from the group consisting of: benzimidazole-2-one-5-n-pentanoate, 5-[2-(1-oxy-2-hydroxyethyl)ethyl]benzimidazol-2-one-5-carboxylate, benzimidazole-2-one-5-methanoate, benzimidazole-2-one-5-ethanoate, 3,4,5-tris(acetyloxy)-6-[(acetyloxy)methyl]tetrahydro-2H-pyran-2-yl-benzimidazole-2-one-5-carboxylate, 5-bromo-6-methylbenzimidazol-2-one, 5-hydroxy-6-methylbenzimidazol-2-one, 5-dodecanylbenzoimidazol-2-one, 4,5,7-tribromo-6-methylbenzimidazol-2-one, 4,5,6,7-tetrabromobenzimidazol-2-one, 5-methyl-6-nitrobenzimidazol-2-one, 5-amino-6-methylbenzimidazol-2-one, N-(6-methylbenzimidazol-5-yl)-2-pyrimidin-2-yl-sulfanyl-acetamide, pentyl-benzimidazol-2-one-5-carbithioate, 5-(benzimidazol-2(3H)-one-6-yl)-5-oxopentanoic acid, 2(3H)-benzimidazolone-5-sulfonic acid pentyl ester, 2(3H)-benzimidazolone-5-sulfonic acid pentyl amide, N-butyl-2-oxo-2,3-dihydro-

1H-1,3-benzimidazole-5-carboximidamide, 5-heptanoylbenzofuran-2(3H)-one, methyl 3-hydroxy-2-{{(2-oxo-2,3-dihydro-1H-1,3-benzimidazol-5-yl)carbonyl}amino}propanoate, 3-hydroxy-2-{{(2-oxo-2,3-dihydro-1H-1,3-benzimidazol-5-yl)carbonyl}amino}propanoic acid, methyl 2-{{(2-oxo-2,3-dihydro-1H-1,3-benzimidazol-5-yl)carbonyl}amino}-3-phenylpropanoate, 2-{{(2-oxo-2,3-dihydro-1H-1,3-benzimidazol-5-yl)carbonyl}amino}-3-phenylpropanoic acid, and N-(3,4-dihydroxyphenethyl)-2-oxo-2,3-dihydro-1H-1,3-benzimidazole-5-carboxamide.

19. (original) A method of treating, preventing or diagnosing a disease or condition wherein MIF cytokine or biological activity is implicated comprising the administration of a treatment, prevention or diagnostic effective amount of a compound of formula (I) as defined in claim 1 or a pharmaceutically acceptable salt or prodrug thereof to a subject in need thereof.

20. (original) A method according to claim 19 wherein the disease or condition is selected from autoimmune diseases, solid or haemopoietic tumours and chronic or acute inflammatory diseases.

21. (original) A method according to claim 19 wherein the disease or condition is selected from the group consisting of Rheumatic diseases, spondyloarthropathies, crystal arthropathies, Lyme disease, connective tissue diseases, vasculitides, glomerulonephritis, interstitial nephritis, inflammatory bowel disease, peptic ulceration, gastritis, oesophagitis, liver disease, autoimmune diseases, pulmonary diseases, cancers whether primary or metastatic, atherosclerosis, disorders of the hypothalamic-pituitary-adrenal axis, brain disorders, corneal

disease, iritis, iridocyclitis, cataracts, uveitis, sarcoidosis, diseases characterised by modified angiogenesis, endometrial function, psoriasis, endotoxic (septic) shock, exotoxic (septic) shock, infective (true septic) shock, other complications of infection, pelvic inflammatory disease, transplant rejection, allergies, allergic rhinitis, bone diseases, atopic dermatitis, UV(B)-induced dermal cell activation, malarial complications, diabetes mellitus, pain, inflammatory consequences of trauma or ischaemia, testicular dysfunctions and wound healing.

22. (original) A method according to claim 21 wherein the disease or condition is selected from the group consisting of rheumatoid arthritis, osteoarthritis, psoriatic arthritis, ankylosing spondylitis, reactive arthritis, Reiter's syndrome, gout, pseudogout, calcium pyrophosphate deposition disease, systemic lupus erythematosus, systemic sclerosis, polymyositis, dermatomyositis, Sjögren's syndrome, polyarteritis nodosa, Wegener's granulomatosis, Churg-Strauss syndrome, ulcerative colitis, Crohn's disease, cirrhosis, hepatitis, diabetes mellitus, thyroiditis, myasthenia gravis, sclerosing cholangitis, primary biliary cirrhosis, diffuse interstitial lung diseases, pneumoconioses, fibrosing alveolitis, asthma, bronchitis, bronchiectasis, chronic obstructive pulmonary disease, adult respiratory distress syndrome, colon cancer, lymphoma, lung cancer, melanoma, prostate cancer, breast cancer, stomach cancer, leukemia, cervical cancer and metastatic cancer, ischaemic heart disease, myocardial infarction, stroke, peripheral vascular disease, Alzheimer's disease, multiple sclerosis, diabetic retinopathy, parturition, endometriosis, osteoporosis, Paget's disease, sunburn and skin cancer.

23. (original) A method of claim 19 wherein the subject is a human subject.

24-25. (cancelled)

26. (original) A method of treating or preventing a disease or condition wherein MIF cytokine or biological activity is implicated comprising: administering to a mammal a compound of formula (I) as defined in claim 1 or a pharmaceutically acceptable salt or prodrug thereof and a second therapeutic agent.

27. (original) A method according to claim 26 wherein the second therapeutic agent is a glucocorticoid.

28. (original) A method of prophylaxis or treatment of a disease or condition for which treatment with a glucocorticoid is indicated, said method comprising: administering to a mammal a glucocorticoid and a compound of formula (I) as defined in claim 1 or a pharmaceutically acceptable salt or prodrug thereof.

29. (original) A method of treating a steroid-resistant disease or condition comprising: administering to a mammal a glucocorticoid and a compound of formula (I) as defined in claim 1 or a pharmaceutically acceptable salt or prodrug thereof.

30. (original) A method of enhancing the effect of a glucocorticoid in mammals comprising administering a compound of formula (I) as defined in claim 1 or a pharmaceutically acceptable salt or prodrug thereof simultaneously, separately or sequentially with said glucocorticoid.

RESPONSE TO RESTRICTION REQUIREMENT
U.S.S.N. 10/517,264

31-40. (canceled)